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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D C 20460

MAY 20 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Agency Comments on the Uniroyal Chemical Company Letter Dated February 5, 1988 on the EPA Lab Audit Report Dated January 25, 1988 - IRDC Lab Studies of Alar and UDMH - No MRID Number Assigned

Caswell No.: 808 ~~3668~~
TOX Br. Proj. No.: 8-0421

FROM: Henry Spencer, Ph.D., Pharmacologist
Toxicology Branch
Hazard Evaluation Division (TS-769C)

8/16/88

TO: Walter Waldrop/Mark Boodee, PM Team 81
Special Review Branch
Registration Division (TS-767C)

THRU: Albin Kocialski, Ph.D., Supervisory Pharmacologist
Review Section VII, Toxicology Branch
Hazard Evaluation Division (TS-769C)

ABK 5/17/88

and

Theodore Farber, Ph.D.
Chief, Toxicology Branch
Hazard Evaluation Division (TS-769C)

5/20/88

Background

The Agency audited the International Research and Development Corporation labs for oncogenicity studies on Alar and UDMH in late 1987. An audit report was sent to the registrant, Uniroyal Chemical Company, dated January 25, 1988. Uniroyal has taken notice of several concerns voiced in the report and has returned comments.

Uniroyal's concerns are listed below with the course of action they have taken, and the Agency's reply.

Concern No. 1

After representative slides were made the remaining liver tissues were discarded.

Company Reply

Instructions and protocol amendments were made to save all tissues from these studies.

Agency Response

The Agency concurs with the registrant's action on saving all the tissues.

Concern No. 2

Stability and homogeneity data on Alar are to be submitted with the final report.

Company Reply

The registrant concurs with the request.

Agency Response

The Agency has no further comments concerning this question.

Concern No. 3

A question of composition and purity of the UDMH test material arose.

Company Reply

The registrant noted that the UDMH was made fresh at Uniroyal Chemical each 3 to 4 weeks, and purity results were included.

Agency Response

The Agency notes receipt of the data and assumes that they will be included in the report.

attachment

CHEMICAL
Bethany, Connecticut 06525
(203) 393-2163

February 5, 1988

Registration Division (TS-767C)
U.S. Environmental Protection Agency
CM #2, 1921 Jefferson Davis Highway
Arlington, Virginia 22202

Attention: Mr. Walter Waldrop, Special Review Branch

Subject: Daminozide - Audit at International Research and Development Corporation

Dear Mr. Waldrop:

We have received a review of the audit by the EPA on the oncogenicity studies with Alar and UDMH at International Research and Development Corporation (IRDC) dated January 25, 1988. Three areas of concern were noted and we would like to clarify these points with this letter.

One concern was that all tissues taken from test animals be saved for future examination, even after microscope slide sections have been made. We believe this concern stems from the IRDC practice of discarding rat (not mouse) livers after representative sections and all lesions are removed. Uniroyal Chemical has instructed IRDC to save all tissues from all studies including the UDMH rat study. A protocol amendment is attached for your review. (Attachment 1). The Alar rat study was complete prior to the EPA audit, and tissues were handled according to the SOP's at the time.

Uniroyal also received word from IRDC that the EPA had requested additional sectioning of mouse livers from the UDMH studies. We will agree to do this extra sectioning. A protocol amendment is attached for your review. (Attachment 2). This change was made for all three UDMH oncogenicity studies. A detailed SOP of how the liver is sectioned is also attached. (Attachment 3).

The second concern raised by EPA was that results from stability and homogenicity tests on the Alar study be included with the final report. The original work by IRDC showed some variance in results. This work has been repeated with better results and will be included with the final report.

The third area of concern was in the purity and composition of the UDMH test material used in the UDMH oncogenicity studies. The UDMH

used in the rat and mouse oncogenicity studies was prepared at Uniroyal Chemical every 3 - 4 weeks. The purity analysis for each batch is performed using a certified standard after that batch arrives at the contract laboratory. Results of the purity analyses for the batches used in the oncogenicity studies are attached. (Attachment 4). These unaudited results were supplied by IRDC.

We hope this letter and enclosed data answer the questions raised by the EPA audit.

Sincerely,

UNIROYAL CHEMICAL COMPANY, INC.

Frederick Hagema FOR

Raymond A. Cardona, Ph.D.
Manager, Registration & Toxicology
Crop Protection Research

cc: Edwin F. Tinsworth, Director
Registration Division

Attachments
Hand carried; receipt requested.

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